AN INSTANCE OF HYPERSENSITIVENESS TO HOMATROPIN.*

By DOUGLASS W. MONTGOMERY, M. D., San Francisco.

A doctor, aged fifty and in excellent health, had a drop of a weak solution of cocaine followed by a wafer containing cocaine and homatropin aa one-fiftieth of a grain, put into his eyes by an oculist on Saturday morning, April 17, 1909. On Sunday afternoon a well-circumscribed, bright red, raised, edematously thickened patch appeared on the penis and scrotum. The patch was very itchy and tinglingly hot. On Monday a red patch appeared on the dorsum of the right foot, having the same characteristics as the condition on the privates. On Tuesday the trouble on the privates continued in the same intensity, and the anus felt dry and hot. On Wednesday morning there appeared two red papular patches over the front of each thigh. The feces were now dry. The small toes of the right foot became red, swollen, hot and itchy, and the sputum was now noticed to be a little stickier than normal. The dilation of the pupils, to accomplish which the drugs had been administered, had by this time almost entirely disappeared. On April 23, six days after the medication, the eruptions and itchiness were rapidly decreasing, but the skin had still a dry, hot feeling, and for two days the tongue had been rough as felt against the palate; it tingled slightly, and there was a sweetish taste in the mouth.

The doctor first thought he was suffering from an attack of poison oak. But as the eruption developed he feared he was going to be a victim of neurotic eczema, a most stubborn affection, and it was a few hours before the true explanation of the trouble became clear.

There can be no doubt that the disturbances in this case were due to the homatropin, although we have no reports of eruptions caused by this drug. It is well known, however, that atropin and the other drugs of its class can give rise to just such eruptions, and, in the case in hand, the symptoms occurred coincidently with the dilation of the pupil and subsided with its contraction, and they were erythematous, and consequently vasodilatory, and therefore in accordance with the vasodilatory eruptions of belladonna and atropin. In fact, the patches on the skin were more characteristically vasomotor in their appearance than most of the eruptions ascribed to belladonna, as they were not alone bright red, but also edematous and circular, their circularity corresponding to the terminal branches of an arteriole tree.

There is a tendency now to ascribe these poisonings to anaphylaxis. In the present instance, however, there was no previous administration of the drug to bring about an artificial sensitiveness. The drug naturally acts as an excitant of the nerves governing respiration and circulation and paralyzes the organs supplied by the autonome nerves,[1] and in the present case these nerves and organs were more than ordinarily sensitive.

A number of instances of poisoning through the instillation of atropin solution into the eye have been reported, but they are relatively rare, considering the frequent use of the drug by oculists. As homatropin is very much weaker than atropin, poisoning by it would be all the more rare, and the symptoms in the present case, arising from its employment as a mydriatic, would indicate a high degree of susceptibility in this patient. If we refer again to our knowledge of atropin and belladonna as enlarging our knowledge of homatropin, we find that the range of tolerant dosage of atropin is very great. Roschtswky relates an instance when one drop of one to one thousand solution of atropin instilled into the eye caused symptoms of intoxication. In another, two drops of a one per cent. solution brought on a crisis of angor pectoris in a patient who previously had suffered from angina of the chest.[2]

Striking peculiarities in this case were the patchy form of the eruption, and its situation on the privates and lower extremities. The picture of acute, severe belladonna poisoning is well known. The pupils are widely dilated, and this, together with the flying pulse, quick breath, incoherent rapid speech, flushed face, that often reddens to the extent of being a scarlatina-like eruption, gives the appearance of wild unbridled forces, resembling the delirium of high fever. When an eruption occurs it is almost always on the face, hands, neck or trunk. In fact, Michelet says it never appears on the extremities.[3] On the other hand, Knowles says that the great majority of cases exhibit the erythematous or scarlatina type of eruption, which is more frequently found on the face or upper portion of the body, but that in a fair number of cases the outbreak is generalized.[4]

The eruption, as indicated above, is almost always diffuse, resembling that of scarlet fever, with which it is often compared. Of a number of text books consulted in studying this case, Stelwagon's is the only one that mentions the occurrence of patchy, erythematous areas or flushings.[5]

The inhibition of the secretions, so well known in belladonna poisoning, was quite marked in this case of homatropin poisoning. The mouth was dry, the skin was dry and uncomfortable, the anal opening felt dry and hot, and the feces became dry. The dryness of the mouth and the dryness of the skin are well known effects of the administration of belladonna, that are taken advantage of therapeutically in controlling both sialorrhea and hyperidrosis. The drying up of the secretions of the stomach and intestines is, however, rarely taken into consideration in giving the drug, and yet it is a most important matter, and undoubtedly often gives rise to what v. Anrep and Marandon de Montyel designate as chronic belladonna poisoning, characterized by loss of appetite, emaciation and loss of weight.[6] Furthermore, it was long ago pointed out by v. Graefe that the continued instillation of atropin into the eye will produce general erethic weakness, and lowering of the power to assimilate food.[7]

Acute constitutional belladonna poisoning is very rare with oculists because the dose employed is very low, and few patients are so highly sensitive to the drug as the one the case of whom is here reported. Oculists, however, run the danger of administering atropin as a mydriatic to patients who are already taking the drug in very considerable doses as an antispasmodic in laxative pills, in

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which case the small additional amount given by the oculist may bring on alarming symptoms.

From what has been said of the danger of chronic constitutional poisoning in the prolonged administration of belladonna, it follows that its daily use in laxative pills may be most fateful in bringing about a lowering of the vital forces and therefore accelerating the symptoms of old age, and inviting bacterial attack. In this way belladonna may render the treatment of a disease of the skin, say of an eczema or a lichen planus, completely nugatory. And in these diseases it is not alone the lowering of the nutrition, but also the belladonna erethism, mentioned by v. Graefe, that is of importance in nullifying all efforts to give relief.

In conclusion it is desired to draw attention to the fact that belladonna and its nearly related plant species and their alkaloids should always be prescribed with a definite object in view, and when this object is attained, or hope of attainment relinquished, the use of the drug should be stopped. In giving the drug for any one object all the other phenomena induced by the drug should be considered, and their occurrence noted. As Michelet says, in giving belladonna it is necessary for the physician to keep his eyes wide open, lest the patient should open his eyes too wide. On no account should this powerful drug, with its wide range of dosage in people of varying susceptibility, be employed regularly and for long spaces of time as an anti-spasmodic in laxative pills, given, as is generally the case, by the physician and taken by the patient as a mere luxury to prevent disagreeable griping, and without any reference whatever to the other actions of the drug.

Discussion.

Dr. E. D. Chipman: We employ powerful drugs many times when something else would answer as well. Such drugs as antimony, known to have a depressing effect on the circulation, are used in acute inflammatory skin diseases when we could arrive at the same result by using Epsom salts.

Dr. J. Cameron Pickett: A case similar to the one cited by Dr. Montgomery came under my observation recently. A young man was sent to me by a general practitioner with an erythematous eczema on both legs and arms, which itched intensely; the skin over the whole body was extremely dry. The case had resisted former treatment. I practically continued the same treatment but stopped the use of a patent "asthma cure," because I had found that the skin symptoms had appeared soon after he had begun taking the "asthma cure." I do not know the constituents of the "cure," but presume that the erythema was due to the presence in it of homatropine or of something similar.

Dr. Montgomery, closing discussion: One of the most important matters in all these cases is the recognition of the eruption as being due to a drug. The symptoms of atropin poisoning are, however, quite well known. One of the most impressive things to me about the present case was the effect of the drug on the alimentary tract. Here it acted as a true hypocrinic, diminishing the secretions through its paralyzing effect on the autonome nerves. If this drug is given as an antispasmodic to stop the griping effect of a laxative pill, it must also act as a hypocrinic. That this hypocrinic action is so slight as not to be appreciated in the daily movements of the bowels is not the point. It may even be masked by that other effect of belladonna in increasing the action of the smooth muscle fibres of the intestines. Diminution of secretions, nevertheless, is present, and being chronic when the drug is chronically given, as in laxative pills, its effects are in my judgment most grave. I am sure in diminishing the secretions of the organs it hastens the phenomena of old age. It is surprising how quickly women will cease using those pills when once informed of this fact.

1 Die Experimentelle Pharmokologie v. H. Meyer u. R. Gottlieb, ii Ed., S. 24 u. 140.
2 Cited by Alfred Martinet in Les Medicaments Usuels, 3d Edition, Page 277.
3 Loc. cit.
4 Generalized Eruptions of Unusual Type Caused by Absorption from a Belladonna Plaster and from the Ocular Instillation of Atropin, by Dr. F. C. Knowles, American Journal of Medical Sciences, July, 1911.
5 Diseases of the Skin, 5th Edition, p. 425.
6 Quoted by Meyer u. Gottlieb. Loc. cit.
7 Graefe's Archiv. 1863, Bd. 9, T. 2, S. 71, also quoted by Meyer u. Gottlieb.

RAYNAUD'S DISEASE—REPORT OF A CASE.*

By LEWIS SAYRE MACE, M. D., San Francisco.

A healthy young woman, 24 years old, applied to the San Francisco Polyclinic complaining of constipation. In the course of her history it developed that she had been troubled for the past two years by attacks of what she called "dead fingers." The first three fingers of each hand would on exposure to cold, or bathing in cold water, become tingling, numb, and finally a dead white and entirely devoid of sensation. In the course of an hour this would pass off, and the peculiar condition occasioned her no discomfort and but little curiosity.

No physical abnormalities were found. Blood and urine were negative, and systolic blood pressure was 120 mm.

This description of dead fingers occurring at intervals, usually on exposure to cold, and affecting the same fingers of each hand, corresponds to the first stage of the disease described by Raynaud in 1862: the stage of local syncope.

The patient before us is a man 48 years old. About a year ago he noticed that upon exposure to cold, or bathing his hands in cold water, certain fingers of each hand would become numb or dead in the manner previously described, but with him the symptoms proceed still further. The fingers, after remaining white and dead for a time, become a dull, deep blue black. No pain is present in this particular instance but the appearance is that of a serious affliction and the imminence of tissue death is apparent. The attacks usually occur most frequently during cold weather or upon bathing with cold water. He may be free for weeks or have several attacks in the course of a day. They are sufficiently annoying to seriously hinder him in the pursuit of his occupation, that of a barber. This condition seems to correspond to the second stage of Raynaud's disease: the stage of local asphyxia.

When tissue death does actually occur, blebs filled with serum appear on the surface of the affected members, areas of superficial necrosis develop, and the third stage, or stage of local gangrene, is present.

On physical examination this patient presents but little of clinical interest. He is 48 years old. His family history is clear, and aside from the ordinary diseases of childhood he has had no illnesses except an attack of jaundice one year ago which lasted two weeks. Urine and blood examinations show no abnormalities and the Wassermann test is not positive. The elimination of urea is not diminished. He has a fairly well marked arteriosclerosis—the radial artery is moderately sclerotic, and the temporal arteries are

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